



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Stavros C. Manolagas, Robert L. Jilka, Robert S. Weinstein, Teresita Bellido,  
Donald Bodenner and Stavroula Kousteni

Application No.: 10/829,028

Group Art Unit: 1614

Filed: April 21, 2004

Examiner: Not yet assigned

Confirmation No.: 5984

Title: METHOD AND COMPOSITIONS FOR INCREASING BONE MASS

<b>CERTIFICATE OF MAILING OR TRANSMISSION</b>	
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INFORMATION DISCLOSURE STATEMENT

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Sir:

This Information Disclosure Statement is submitted:

☐ under 37 CFR 1.129(a), or  
(First/Second submission after Final Rejection)

☒ under 37 CFR 1.97(b), or  
(Within any one of the following time periods: three months of filing national application (other than a CPA) or date of entry of the national stage in an international application; or before the mailing date of a first office action on the merits in a non-provisional application, including a CPA, or a Request for Continued Examination).

☐ under 37 CFR 1.97(c) together with either:  
☐ a Statement under 37 CFR 1.97(e), as checked below, or  
☐ a \$180.00 fee under 37 CFR 1.17(p), or  
(After the 37 CFR 1.97(b) time period, but before final action or notice of allowance, whichever occurs first)

☐ under 37 CFR 1.97(d) together with:  
☐ a Statement under 37 CFR 1.97(e), as checked below, and  
☐ a \$180.00 fee under 37 CFR 1.17(p), or  
(Filed after final action or notice of allowance, whichever occurs first, but on or before payment of the issue fee)

☐ under 37 CFR 1.97(i):  
Applicant requests that the IDS and cited reference(s) be placed in the application filewrapper.  
(Filed after payment of issue fee)

Statement Under 37 CFR 1.97(e)

- ☐ Each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement; or
- ☐ No item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the undersigned, after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of this Information Disclosure Statement.

Statement Under 37 CFR 1.704(d) (Patent Term Adjustment)

Applies to original applications (other than design) filed on or after May 29, 2000

- ☐ Each item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart application and this communication was not received by any individual designated in § 1.56(c) more than thirty days prior to the filing of the Information Disclosure Statement.
- ☒ Enclosed herewith is form PTO-1449:
- ☒ Copies of the cited references are enclosed.
- ☒ Since this application was filed after June 30, 2003, copies of issued U.S. patents and published U.S. applications are not required and are not being provided.
- ☒ Copies of the cited references are enclosed except those entered in prior application, U.S. Application No. 09/414,091, to which priority under 35 U.S.C. 120 is claimed. The earlier application contains copies of the cited references.
- ☐ The listed references were cited in the enclosed International Search Report in a counterpart foreign application.
- ☐ The "concise explanation" requirement (non-English references) for reference(s) ☐ under 37 CFR 1.98(a)(3) is satisfied by:
- ☐ the explanation provided on the attached sheet.
- ☐ the explanation provided in the Specification.
- ☐ submission of the enclosed International Search Report.
- ☐ submission of the enclosed English-language version of a foreign Search Report and/or foreign Office Action.
- ☐ the enclosed English language abstract.

☐ Applicant requests that the following non-published pending applications be considered:

Examiner's  
Initials

\_\_\_\_\_ U.S. Patent Application No. [ ], by [inventor(s)], filed [ ], Docket No.: [ ]

\_\_\_\_\_ U.S. Patent Application No. [ ], by [inventor(s)], filed [ ], Docket No.: [ ]

\_\_\_\_\_ U.S. Patent Application No. [ ], by [inventor(s)], filed [ ], Docket No.: [ ]

\_\_\_\_\_  
Examiner

\_\_\_\_\_  
Date

☐ A copy of each above-cited application, including the current claims, is enclosed.

☐ A copy of each above-cited application, including the current claims, is enclosed, except those entered in prior application, U.S. Application No. [ ], to which priority under 35 U.S.C. 120 is claimed.

The Examiner is requested to return a copy of the above list of pending applications indicating which references were considered with the next office communication.

It is requested that the information disclosed herein be made of record in this application.

Method of payment:

☐ A check for the fee noted above is enclosed, or the fee has been included in the check with the accompanying Reply. A copy of this Statement is enclosed.

☐ Please charge Deposit Account 08-0380 in the amount of \$[ ]. A copy of this Statement is enclosed.

☒ Please charge any deficiency in fees and credit any overpayment to Deposit Account 08-0380.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By Pamela A. Torpey

Pamela A. Torpey

Registration No.: 45,736

Telephone: (978) 341-0036

Facsimile: (978) 341-0136

Concord, MA 01742-9133

Dated:

September 30, 2004

PTO-1449 REPRODUCED		ATTORNEY DOCKET NO. 3650.1006-010		APPLICATION NO. 10/829,028	
<b>INFORMATION DISCLOSURE CITATION IN AN APPLICATION</b>  September 30, 2004 (Use several sheets if necessary)		FIRST NAMED INVENTOR Stavros C. Manolagas		FILING DATE April 21, 2004	
				EXAMINER Not yet assigned	



U.S. PATENT DOCUMENTS				
EXAM- INER INI- TIAL	REF. NO.	DOCUMENT NUMBER Number-Kind Code (if known)	ISSUE DATE / PUBLICATION DATE MM-DD-YYYY	NAME OF PATENTEE OR APPLICANT OF CITED DOCUMENT
	AA	5,885,973	03/23/1999	Papapoulos, <i>et al.</i>
	AB	5,859,001	01/12/1999	Simpkins, <i>et al.</i>
	AC	5,843,934	12/01/1998	Simpkins
	AD	5,824,672	10/20/1998	Simpkins, <i>et al.</i>
	AE	5,753,649	05/19/1998	Tahara, <i>et al.</i>
	AF	5,750,746	05/12/1998	DeLuca, <i>et al.</i>
	AG	5,674,844	10/07/1997	Kuberasampath, <i>et al.</i>
	AH	5,663,195	09/02/1997	Scolnick
	AI	5,618,549	04/08/1997	Patat, <i>et al.</i>
	AJ	5,604,259	02/18/1997	Jee
	AK	5,593,988	01/14/1997	Tahara, <i>et al.</i>
	AA2	5,593,833	01/14/1997	Morrison, <i>et al.</i>
	AB2	5,565,444	10/15/1996	Mizushima, <i>et al.</i>
	AC2	5,532,391	07/02/1996	DeLuca, <i>et al.</i>
	AD2	5,532,226	07/02/1996	Demarest, <i>et al.</i>
	AE2	5,510,370	04/23/1996	Hock
	AF2	5,414,098	05/09/1995	DeLuca, <i>et al.</i>
	AG2	5,403,831	04/04/1995	DeLuca, <i>et al.</i>
	AH2	5,354,773	10/11/1994	Herslof, <i>et al.</i>
	AI2	5,300,687	04/05/1994	Schwender, <i>et al.</i>
	AJ2	5,260,290	11/09/1993	DeLuca, <i>et al.</i>
	AK2	5,208,219	05/04/1993	Ogawa, <i>et al.</i>
	AA3	5,183,815	02/02/1993	Saari, <i>et al.</i>
	AB3	5,164,368	11/17/1992	Recker
	AC3	5,140,864	04/14/1992	DeLuca, <i>et al.</i>
	AD3	5,118,667	06/02/1992	Adams, <i>et al.</i>

EXAMINER	DATE CONSIDERED
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PTO-1449 REPRODUCED  <b>INFORMATION DISCLOSURE CITATION IN AN APPLICATION</b>  <b>September 30, 2004</b>  (Use several sheets if necessary)	ATTORNEY DOCKET NO. 3650.1006-010		APPLICATION NO. 10/829,028	
	FIRST NAMED INVENTOR Stavros C. Manolagas		FILING DATE April 21, 2004	
	EXAMINER Not yet assigned		CONFIRMATION NO. 5984	GROUP 1614

U.S. PATENT DOCUMENTS				
EXAM- INER INI- TIAL	REF. NO.	DOCUMENT NUMBER Number-Kind Code (if known)	ISSUE DATE / PUBLICATION DATE MM-DD-YYYY	NAME OF PATENTEE OR APPLICANT OF CITED DOCUMENT
	AE3	5,071,655	12/10/1991	Baylink
	AF3	5,001,118	03/19/1991	Maeda, <i>et al.</i>
	AG3	4,973,584	11/27/1990	DeLuca, <i>et al.</i>
	AH3	4,970,237	11/13/1990	Jensen, <i>et al.</i>
	AI3	4,870,063	09/26/1989	Binderup, <i>et al.</i>
	AJ3	4,870,054	09/26/1989	Recker
	AK3	4,833,125	05/23/1989	Neer, <i>et al.</i>
	AA4	4,710,382	12/01/1987	Recker
	AB4	4,619,920	10/28/1986	DeLuca, <i>et al.</i>
	AC4	4,588,716	05/13/1986	DeLuca, <i>et al.</i>
	AD4	4,522,811	06/11/1985	Eppstein, <i>et al.</i>
	AE4	5,362,720	11/08/1994	Labrie
	AF4	5,189,212	02/23/1993	Ruenitz
	AG4	5,071,773	12/10/1991	Evans, <i>et al.</i>
	AH4	5,298,429	03/29/1994	Evans, <i>et al.</i>
	AI4	5,545,634	08/13/1996	Labrie, <i>et al.</i>
	AJ4	5,506,102	04/09/1996	McDonnell
	AK4	5,554,601	09/10/1996	Simpkins, <i>et al.</i>
	AA5	5,567,695	10/22/1996	Labrie
	AB5	5,846,960	12/08/1998	Labrie
	AC5	5,877,007	03/02/1999	Housey
	AD5	6,080,779	06/27/2000	Gaspar, <i>et al.</i>
	AE5	6,319,914	11/20/2001	Simpkins, <i>et al.</i>
	AF5	6,011,027	01/04/2000	Arnold
	AG5	5,880,117	03/09/1999	Arnold

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<b>PTO-1449 REPRODUCED</b>  <b>INFORMATION DISCLOSURE CITATION IN AN APPLICATION</b>  <b>September 30, 2004</b>  (Use several sheets if necessary)	<b>ATTORNEY DOCKET NO.</b> 3650.1006-010		<b>APPLICATION NO.</b> 10/829,028	
	<b>FIRST NAMED INVENTOR</b> Stavros C. Manolagas		<b>FILING DATE</b> April 21, 2004	
	<b>EXAMINER</b> Not yet assigned		<b>CONFIRMATION NO.</b> 5984	<b>GROUP</b> 1614

FOREIGN PATENT DOCUMENTS						
		DOCUMENT NUMBER Country Code-Number-Kind Code (if known)	DATE MM-DD-YYYY	NAME OF PATENTEE OR APPLICANT OF CITED DOCUMENT	TRANSLATION YES NO	
	AL	WO 98/22113	05/28/1998	Univ. of Florida Research Foundation		
	AM	WO 98/31381	07/23/1998	Univ. of Florida Research Foundation		
	AN	WO 95/26719	10/12/1995	Arcturus Pharmaceutical Corp.		
	AO	EP 0 753 523 A1	01/15/1997	Gador S.A.		
	AP	WO 00/19823 A1	04/13/2000	The Board of Trustees of the University of Arkansas		
	AQ	WO 00/20007 A1	04/13/2000	The Board of Trustees of the University of Arkansas		
	AL2	WO 00/20625 A1	04/13/2000	The Board of Trustees of the University of Arkansas		
	AM2	WO 00/37681 A1	06/29/2000	American Home Products Corporation		
	AN2	WO 99/54728 A3	10/28/1999	Novalon Pharmaceuticals Corporation		
	AO2	WO 99/61044 A	12/02/1999	The Board of Trustees of the University of Arkansas		

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	EXAMINER Not yet assigned		CONFIRMATION NO. 5984	GROUP 1614

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
AR	Bellido, T., <i>et al.</i> , "Overexpression of Bcl-2 Renders Osteoblastic Cells Refractory to Glucocorticoid-Induced Apoptosis", <i>Bone</i> , 23:S324 (1998).	
AS	Bellido, T., <i>et al.</i> , "Regulation of Interleukin-6, Osteoclastogenesis, and Bone Mass by Androgens", <i>J. Clin. Invest.</i> , 95:2886-2895 (1995).	
AT	Berggren, M., <i>et al.</i> , "Glutathione Biosynthesis in the Isolated Perfused Rat Lung: Utilization of Extracellular Glutathione", <i>Federation European Biochemical Societies</i> , 176:189-192 (1984).	
AU	Dempster, D.W., "Exploiting and Bypassing the Bone Remodeling Cycle to Optimize the Treatment of Osteoporosis", <i>J. of Bone and Mineral Research</i> , 12:1152-1154 (1997).	
AV	Dempster, D.W., "New Concepts in Bone Remodeling", <i>Dynamics of Bone and Cartilage Metabolism</i> , Academic Press, 261-273 (1999).	
AW	Ellis, E.F., <i>et al.</i> , "Restoration of Cerebrovascular responsiveness to Hyperventilation by the Oxygen Radical Scavenger N-Acetylcysteine Following Experimental Traumatic Brain Injury", <i>J. of Neurosurgery</i> , 75:774-779 (1991).	
AX	Ettinger, B., <i>et al.</i> , "Reduction of Vertebral Fracture Risk in Postmenopausal Women with Osteoporosis Treated with Raloxifene", <i>J. of the American Medical Association</i> , 282:637-645 (1999).	
AY	Fitzpatrick, L.A., "Selective Estrogen Receptor Modulators and Phytoestrogens: New Therapies for the Postmenopausal Women", <i>Mayo Clin. Proc.</i> , 74:601-607 (1999).	
AZ	Hughes, D.E., <i>et al.</i> , "Estrogen Promotes Apoptosis of Murine Osteoclasts Mediated by TGF- $\beta$ ", <i>Nature Medicine</i> , 2:10:1132-1136 (1996).	
AR2	Jilka, R.L., <i>et al.</i> , "Osteoblast Programmed Cell Death (Apoptosis): Modulation by Growth Factors and Cytokines", <i>J. of Bone and Mineral Research</i> , 13:793-802 (1998).	
AS2	Jilka, R.L., <i>et al.</i> , "Increased Osteoclast Development After Estrogen Loss: Mediation by Interleukin-6", <i>Science</i> , 257:88-91 (1992).	
AT2	Jilka, R.L., <i>et al.</i> , "Linkage of Decreased Bone Mass with Impaired Osteoblastogenesis in a Murine Model of Accelerated Senescence", <i>The Journal of Clinical Investigation</i> , 97:1732-1740 (1996).	

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<b>PTO-1449 REPRODUCED</b>  <b>INFORMATION DISCLOSURE CITATION IN AN APPLICATION</b>  <b>September 30, 2004</b>  (Use several sheets if necessary)	ATTORNEY DOCKET NO. <b>3650.1006-010</b>		APPLICATION NO. <b>10/829,028</b>	
	FIRST NAMED INVENTOR <b>Stavros C. Manolagas</b>		FILING DATE <b>April 21, 2004</b>	
	EXAMINER <b>Not yet assigned</b>		CONFIRMATION NO. <b>5984</b>	GROUP <b>1614</b>

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
AU2	Jilka, R.L., <i>et al.</i> , “Loss of Estrogen Upregulates Osteoblastogenesis in the Murine Bone Marrow, Evidence of Autonomy from Factors Released during Bone Resorption”, <i>The American Society for Clinical Investigation, Inc.</i> , 101:1942-1950 (1998).	
AV2	Jilka, R.L., <i>et al.</i> , “Increased Bone Formation by Prevention of Osteoblast Apoptosis with Parathyroid Hormone”, <i>The Journal of Clinical Investigation</i> , 104:439-446 (1999).	
AW2	Kameda, T., <i>et al.</i> , “Estrogen Inhibits Bone Resorption by Directly Inducing Apoptosis of the Bone-resorbing Osteoclasts”, <i>The Journal of Experimental Medicine</i> , 186:489-495 (1997).	
AX2	Knight, K.R., <i>et al.</i> , “Enhancement of Ischaemic Rabbit Skin Flap Survival with the Antioxidant and Free-Radical Scavenger N-Acetylcysteine”, <i>Clinical Science</i> , 81:31-36 (1991).	
AY2	Lalitha, T., <i>et al.</i> , “Effect of N-acetyl-cysteine, D-Penicillamine and Buthionine Sulfoximine on Glutathione Levels and CNS Oxygen Toxicity in Rats”, <i>Pharmacology &amp; Toxicology</i> , 66:56-61 (1990).	
AX2	Manolagas, S.C., <i>et al.</i> , “Bone Marrow, Cytokines, and Bone Remodeling: Emerging Insights into the Pathophysiology of Osteoporosis”, <i>New England Journal of Medicine</i> , 332:305-311 (1995).	
AR3	Norris, J.D., <i>et al.</i> , “Peptide Antagonists of the Human Estrogen Receptor”, <i>Science</i> , 285(5428):744-746 (1999).	
AS3	Paige, L.A., <i>et al.</i> , “Estrogen Receptor (ER) Modulators Each Induce Distinct Conformational Changes in ER and ER ”, <i>Proc. Natl. Acad. Sci.</i> , 96:3999-4004 (1999).	
AT3	Parfitt, A.M., “Bone-Forming Cells in Clinical Conditions”, <i>Bone</i> , (The osteoblast and osteocyte), CRC Press, Boca Raton, 1:351-430 (1996).	
AU3	Plotkin, L.I., <i>et al.</i> , “Bisphosphonates Prevent Glucocorticoid-Induced Apoptosis of Osteocytes in Vitro: a Putative Mechanism Influencing Mechanosensing”, <i>Bone</i> , 23:S157 (1998).	
AV3	Raisz, L.G., “Estrogen and Bone: New Pieces to the Puzzle”, <i>Nature Medicine</i> , 2:1077-1078 (1996).	
AW3	Smilkstein, M.J., <i>et al.</i> , “Efficacy of Oral N-Acetylcysteine in the Treatment of Acetaminophen Overdose”, <i>The New England Journal of Medicine</i> , 319:1557-1562 (1988).	
AX3	Snyder, P.J., <i>et al.</i> , “Effect of Testosterone Treatment on Bone Mineral Density in Men Over 65 Years of Age”, <i>J. Clin. Endocrin. Metab.</i> , 84:1966-1972 (1999).	

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	EXAMINER Not yet assigned		CONFIRMATION NO. 5984	GROUP 1614

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
AY3	Sun, J., <i>et al.</i> , "Novel Ligands that Function as Selective Estrogens or Antiestrogens for Estrogen Receptor- or Estrogen Receptor", <i>Endocrinology</i> , 140:800-804 (1999).	
AZ3	Weinstein, R.S., <i>et al.</i> , "The Effects of Androgen Deficiency on Murine Bone Remodeling and Bone Mineral Density are Mediated via Cells of the Osteoblastic Lineage", <i>Endocrinology</i> , 138:4013-4021 (1997).	
AR4	Weinstein, R.S., <i>et al.</i> , "Inhibition of Osteoblastogenesis and Promotion of Apoptosis of Osteoblasts and Osteocytes by Glucocorticoids", <i>The Journal of Clinical Investigation</i> , 102:274-282 (1998).	
AS4	Weinstein, R.S., <i>et al.</i> , "Anatomic Juxtaposition of Apoptotic Osteocytes and Avascular Necrosis in Femurs from Patients with Glucocorticoid Excess", <i>Bone</i> , 23:S461 (1998).	
AT4	Catalogue from Steroids, Inc. PO Box 310, Wilton, NH 03086 (undated).	
AU4	Sparks, A.B., <i>et al.</i> , "Screening phage-displayed peptide libraries", <i>Phage Display of Peptides and Proteins, A Laboratory Manual</i> , Academic Press, San Diego, 227-253 (1996).	
AV4	Alessi, D.R., <i>et al.</i> , "PD 098059 Is a Specific Inhibitor of the Activation of Mitogen-activated Protein Kinase in Vitro and In Vivo", <i>J. Biol. Chem.</i> , 270:27489-27494 (1995).	
AW4	Bellido, T., <i>et al.</i> , "Activation of the Janus Kinase/STAT (Signal Transducer and Activation of Transcription) Signal Transduction Pathway by Interleukin-6-Tye Cytokines Promotes Osteoblast Differentiation", <i>Endocrinology</i> , 138:3666-3676 (1997).	
AX4	Falkenstein, E., <i>et al.</i> , "Nongenomically initiated steroid actions", <i>Eur J Clin Invest.</i> , Suppl, 3:51-54 (2000).	
AY4	Finkel, E., "Phyto-oestrogens: the way postmenopausal health", <i>The Lancet</i> , 352(9142): 1762 (1998).	
AZ4	Hill, P.A., <i>et al.</i> , "Multiple extracellular signals promote osteoblast survival and apoptosis", <i>Endocrinology</i> , 138(9): 3849-3858 (1997).	
AR5	Kato, Y., <i>et al.</i> , "Establishment of an Osteocyte-like Cell Line, MLO-Y4", <i>Journal of Bone and Mineral Research</i> , 12:2014-2023 (1997).	
AS5	Parfitt, A.M., "Calcitriol for postmenopausal osteoporosis", <i>Ann Intern Med.</i> , 112(2):147 (1990).	

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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
	AT5	Xia, Z., <i>et al.</i> , "Opposing Effects of ERK and JNK-p38 MAP Kinases on Apoptosis", <i>Science</i> , 270:1326-1331 (1995).

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